

Award Number: W81XWH-16-1-0763

TITLE: Increasing Bone Mass and Bone Strength in Individuals with Chronic Spinal Cord Injury: Maximizing Response to Therapy

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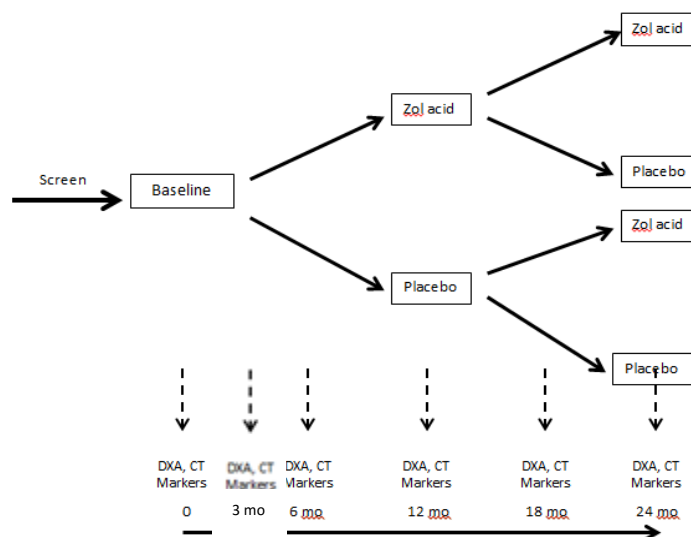
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14. ABSTRACT Rapid bone loss is a universal accompaniment of acute spinal cord injury (SCI) and leads to severe loss of bone mass and bone strength with a marked increased risk of fracture. This 24 month double-blind, randomized, placebo-controlled study evaluates in 60 participants the efficacy (bone mass and bone strength) and safety of zoledronic acid administered early after acute SCI to prevent bone loss, the duration of its effects and the value of using biomarkers to guide therapy. Data collection (bone imaging and biomarkers) occurs at baseline and after 3, 6 and 12 months during the first year; participants are re-randomized after 12 months with subsequent data collection at 18 and 24 months. Currently, all regulatory requirements for the study have been completed. Fifty-one (51) participants have been randomized and treated. No unexpected safety events have occurred. Data collection is on-going and additional patients are being screened for study entry.					
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INTRODUCTION:

Rapid bone loss is a universal accompaniment of acute spinal cord injury (SCI) and leads to severe loss of bone mass and bone strength with a marked increased risk of fracture. The study proposed is a 2 year, randomized, double-blind placebo-controlled study of zoledronic acid to evaluate its efficacy and safety for the prevention of bone loss and maintenance of bone strength in individuals with recent onset SCI (see diagram below). At the end of the first year of the study, each treatment groups will be re-randomized to either zoledronic acid or placebo to evaluate the durability of response to zoledronic acid and the utility of serum bone markers to guide therapeutic decision making. DXA imaging, CT imaging and bone markers will be obtained at baseline, 3 months, 6 months, 12 months, 18 months and 24 months.



KEYWORDS: spinal cord injury, bone mass, bone strength, osteoporosis, zoledronic acid

OVERALL PROJECT SUMMARY:

All objectives outlined in the Statement of Work to be completed during the third year have been completed or are on-going. All regulatory approvals have been maintained. Screening, enrollment and treatment of participants (Specific Aim 1, Major Task 3) continues, with 51 participants currently randomized and active in the study. Data are being obtained and entered into the study database, and study materials are being collected and maintained for future assay (biomarkers; part of Specific Aim 2, Major Task 1) or for image analysis (CT bone scans; part of Specific Aim 3, Major Task 1). As the investigators remain blinded to allocation of treatment assignment, it is not possible to know efficacy results until the end of the study. Safety is being continually monitored by collection of adverse events. The medical monitor continues to review all AEs and study procedures at the regularly held data safety monitoring committee meetings. No safety concerns have been identified and no changes in the study proposed.

Recruitment has been largely on track after a delayed start due to a longer time required to obtain regulatory approvals than was anticipated. The only significant impediment to recruitment has been the move of the Rehabilitation Institute of Chicago into a new physical facility one block away, now named the Shirley Ryan AbilityLab (SRLab). Hospital administration suspended our in-patient research

activities at the new facility for a period of 3 months pending clinical operations being stabilized and our staff's completing orientation. During the 3 months when we could not recruit new participants, we continued to follow previously enrolled participants and collected all required data at their return visits. Recruitment and enrollment have now been restarted, and treatment and data collection are proceeding without further issues. All participants enrolled after the move to SRAlab will have all of their DXA and CT scans performed at SRAlab as SRAlab patients are not allowed to leave the hospital, as they had before, for procedures. No changes have been made in the statement of work and only minor modifications of the protocol and informed consent have been made.

KEY RESEARCH ACCOMPLISHMENTS:

There are no outcome data available to date. As this is a blinded clinical trial, scientific data relating to study objectives will not be available until all participants have concluded the study, data cleaned and data base locked, and analyses completed.

CONCLUSION:

This project has not progressed to the point of being able to provide any conclusions in regard to the effect of these specific interventions on bone mass or bone quality in people after spinal cord injury. If benefit is shown, this intervention has the potential to reduce fracture incidence in people experiencing acute SCI.

PUBLICATIONS, ABSTRACTS AND PRESENTATIONS:

None.

INVENTIONS, PATENTS AND LICENSES:

None.

REPORTABLE OUTCOMES:

None.

OTHER ACHIEVEMENTS:

None.

REFERENCES:

None.

APPENDICES:

None.

Prevention of Bone Loss after Acute SCI by Zoledronic Acid: Durability, Effect on Bone Strength and Use of Biomarkers to Guide Therapy

Proposal Log Number SC130125; Award # W81XWH-14-2-0193; HRPO Log A-18350



PI: Dr. Thomas J. Schnitzer **Org:** Northwestern University Feinberg School of Medicine

Award Amount: \$2,011,846

Study/Product Aims

- Define timing and frequency of administration of zoledronic acid that will result in optimal prevention of bone loss after acute SCI.
- Evaluate the use of serum markers of bone metabolism to guide therapeutic decisions of timing and need for retreatment with zoledronic acid after acute SCI.
- Evaluate effects of zoledronic acid in mitigating loss of bone strength that occurs after acute SCI.

Approach

This is a 2 year, randomized, double-blind placebo-controlled study. Subjects will be randomized at baseline and again at 12 months to receive either zoledronic acid or placebo each time. Subject will be followed for 24 months with repeat DXA scans, CT scans, and serum bone markers.



Prevent Bone Loss
to Prevent Fractures

IRB approval received at all sites. Recruitment and enrollment continues. Fifty-one subjects have been enrolled.

Timeline and Cost

Activities	CY	14	15	16	17	18
Study Start-Up Activities		■				
Participant Enrollment			■■■■■	■■■■■	■	
Data Collection and Entry			■■■■■	■	■	■
Data Analysis					■	■
Estimated Budget (\$K)		\$138K	\$541K	\$503K	\$465K	\$365K

Goals/Milestones

CY14 Goals – Begin study start-up

- Obtain regulatory approval at all sites

CY15 Goal – Complete start-up, Begin recruitment and enrollment

- Enroll 25-30 subjects into study

CY16 Goal – Continue recruitment and enrollment

- Enroll 25-30 subjects into study

CY17 Goal – Complete subject enrollment

CY18 Goal – Complete data collection and data analysis

- Final study report

Comments/Challenges/Issues/Concerns

- Delayed HRPO approval and RIC hospital move delayed projected timelines
- Enrollment continues but remains behind original estimates
- Under budget to allow for longer recruitment period and followup

Budget Expenditure to Date (September, 2017)

Projected Expenditure: \$1,546,040

Actual Expenditure: \$949,340 (subcontract invoices outstanding)

Updated: 17 October 2017